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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,521	03/19/2001	Caroline Kreutzer	P 278416 980183 BT-CIP	6186
909	7590	01/21/2004	EXAMINER	
PILLSBURY WINTHROP, LLP P.O. BOX 10500 MCLEAN, VA 22102			RAMIREZ, DELIA M	
			ART UNIT	PAPER NUMBER
			1652	
DATE MAILED: 01/21/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/810,521

Applicant(s)

KREUTZER ET AL.

Examiner

Delia M. Ramirez

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 14 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3,16,22,23,27,28 and 30-32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 3,16,22 and 23 is/are allowed.
- 6) ☒ Claim(s) 27,28,31 and 32 is/are rejected.
- 7) ☒ Claim(s) 1 and 30 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 3/19/2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of the Application***

Claims 1, 3, 16, 22-23, 27-28, 30-32 are pending.

Applicant's amendment of claims 1, 3, 16, 27, 28, 30-32, and cancellation of claims 5-15, 17, 18, 21, 24-26, 29 in a communication filed on 10/14/2003 are acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### ***Claim Objections***

1. Claims 1 and 30 remains objected to due to the recitation of "dapA promotor". See line 3 of item b) in both claims. It should be replaced with "dapA promoter". Appropriate correction is required.
2. Claim 1 is objected to due to the recitation of "wherein said overexpression.....gives a pyruvate carboxylase activity or dihydrodipicolinate synthase activity above the level...". For clarity, it is suggested that the term "gives a..." be replaced with "results in pyruvate carboxylase activity or dihydrodipicolinate synthase activity which is above the level...." or similar. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:  
  
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
4. Claim 31-32 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
5. Claims 31-32 are indefinite due to the recitation of the term "overexpressed". As indicated previously, this is a relative term and the specification fails to define the term. For examination purposes,

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it will be assumed that the term refers to a gene which is expressed at a level which is higher than its normal expression level in a wild-type *C. glutamicum*. Correction is required.

***Claim Rejections - 35 USC § 112, First Paragraph***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 27-28 and 31-32 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has been discussed at length in Paper No. 24, mailed on 6/3/2003.

8. Applicant's argue that the current amendments render this rejection moot.

9. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. Claims 27 as amended is directed to the bacterium of claim 1 modified in any way such that the *C. glutamicum* *lysC* gene is expressed at levels which are higher than those found in wild type *C. glutamicum*. Claim 28 is directed to the bacterium of claim 1 modified in any way such that a mutant *C. glutamicum* *lysC* gene is expressed at high levels, wherein said mutant *lysC* gene has been modified in any way to encode an aspartate kinase resistant to inhibition by lysine and/or threonine. Claim 31 is directed to the bacterium of claim 30 modified in any way such that the *C. glutamicum* *lysC* gene is expressed at levels which are higher than those found in wild type *C. glutamicum*. Claim 32 is directed to the bacterium of claim 30 modified in any way such that a mutant *C. glutamicum* *lysC* gene is expressed at high levels, wherein said mutant *lysC* gene has been modified in any way to encode an aspartate kinase resistant to inhibition by lysine and/or threonine.

While it is agreed that the claims as amended are now limited to *C. glutamicum* lysC genes, as indicated in previous Paper No. 24, the claims are still directed to bacterium wherein the *C. glutamicum* lysC gene, or mutant thereof, is overexpressed by any means and not just by increasing the gene copy number. It is reiterated herein that the specification fails to disclose which mutations in the promoter, regulatory region or the ribosome binding site of the recited genes will result in increased expression of said genes. In addition, it is noted that while the specification discloses that a mutant *C. glutamicum* lysC gene encoding an aspartate kinase which is resistant to inhibition by lysine and/or threonine is disclosed in EP-B-0 387 527, the specification fails to disclose which is the structure of said mutant lysC gene or the mutant aspartate kinase encoded by it. Furthermore, while the claims encompass a genus of mutant *C. glutamicum* lysC genes, no disclosure of other structural modifications in the *C. glutamicum* lysC gene which would result in the corresponding aspartate kinase to be resistant to inhibition by lysine and/or threonine have been disclosed. Therefore, in view of the fact that the instant disclosure does not provide sufficient description of (1) a representative number of species of the genus of mutant *C. glutamicum* lysC genes encompassed by the claims, and (2) representative number of modifications such that the expression of the desired gene is increased, one cannot reasonably conclude that the claimed invention is adequately described.

10. Claims 27-28 and 31-32 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a *C. glutamicum* cell wherein the wild type *C. glutamicum* pyc gene, wild type *C. glutamicum* dapA gene, wild type *C. glutamicum* lysE gene, and the wild type *C. glutamicum* lysC gene are overexpressed by increasing the copy number of such genes, does not reasonably provide enablement for a *C. glutamicum* cell further capable of overexpressing the *C. glutamicum* lysC gene by any means or (2) said *C. glutamicum* cell further capable of overexpressing a *C. glutamicum* lysC gene which has been modified in any way to encode an aspartate kinase which is

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resistant to inhibition by lysine and/or threonine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection has been discussed at length in Paper No. 24, mailed on 6/3/2003.

11. Applicant's argue that the current amendments render this rejection moot.

12. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. The scope of the instant claims have been described above. As indicated previously, while the specification discloses overexpression by increasing the copy number of the gene of interest, there is no teaching as to which modifications in the promoter, regulatory region or the ribosome binding site of the recited genes will result in increased expression of said genes. Furthermore, as indicated above, the specification fails to disclose the structural modifications in the *C. glutamicum* lysC gene which are associated with resistance to inhibition by lysine and/or threonine nor does it provide the structure of the mutant *C. glutamicum* lysC gene referred to in the specification as disclosed in EP-B-0 387 527.

Therefore, in view of the lack of information as to (1) which modifications can be made to the regulatory region, promoter or the ribosome binding site of the recited genes to increase their expression, and (2) which are the structural modifications that can be made to the *C. glutamicum* lysC gene such that the corresponding aspartate kinase is resistant to inhibition by lysine and/or threonine, one cannot reasonably conclude that the full scope of the claimed invention is enabled by the disclosure.

***Claim Rejections - 35 USC § 103***

13. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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14. Claims 30-32 were rejected under 35 U.S.C. 103(a) as being unpatentable over Peters-Wendisch et al. (DE 198-31-609-A1, cited in the IDS) in view of Cremer et al. (EP-0-435-132-A1, cited in the IDS), Vrljic et al. (DE 195-48-222-A1, cited in the IDS), and Araki et al.. (EP 0-854-189-A2, cited in the IDS).

15. Claims 30-32 as amended are now directed to a method of producing L-lysine with *C. glutamicum* by increasing the copy number of the wild type *C. glutamicum* *pyc* gene, overexpressing the wild type *C. glutamicum* *dapA* gene with promoters comprising SEQ ID NO: 5 or 6, and overexpressing the wild type *C. glutamicum* *lysE* gene by increasing its copy number. Since neither Wendisch et al., Cremer et al., Vrljic et al., nor Araki et al. alone or in combination teach *dapA* promoters comprising SEQ ID NO: 5 or 6, this rejection is hereby withdrawn.

#### ***Double Patenting***

16. Claim 30 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 3. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

#### ***Allowable Subject Matter***

17. Claims 1, 3, 16, 22, 23 and 30 appear to be allowable over the prior art of record.

#### ***Conclusion***

18. Applicant's amendment of claims 1, 3, 16, 27, 28, 30-32 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

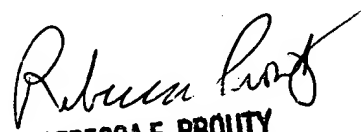
19. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.  
Patent Examiner  
Art Unit 1652

DR  
December 29, 2003

  
REBECCA E. PROUTY  
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1620